



General

Guideline Title

Sentinel lymph node biopsy for melanoma: American Society of Clinical Oncology and Society of Surgical Oncology joint clinical practice guideline.

Bibliographic Source(s)

Wong SL, Balch CM, Hurley P, Agarwala SS, Akhurst TJ, Cochran A, Cormier JN, Gorman M, Kim TY, McMasters KM, Noyes RD, Schuchter LM, Valsecchi ME, Weaver DL, Lyman GH. Sentinel lymph node biopsy for melanoma: American Society of Clinical Oncology and Society of Surgical Oncology joint clinical practice guideline. J Clin Oncol. 2012 Aug 10;30(23):2912-8. [98 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [December 14, 2016 – General anesthetic and sedation drugs](#) : The U.S. Food and Drug Administration (FDA) is warning that repeated or lengthy use of general anesthetic and sedation drugs during surgeries or procedures in children younger than 3 years or in pregnant women during their third trimester may affect the development of children's brains. Consistent with animal studies, recent human studies suggest that a single, relatively short exposure to general anesthetic and sedation drugs in infants or toddlers is unlikely to have negative effects on behavior or learning. However, further research is needed to fully characterize how early life anesthetic exposure affects children's brain development.

Recommendations

Major Recommendations

Clinical Question 1

What Are the Indications for Sentinel Lymph Node (SLN) Biopsy?

Intermediate-Thickness Melanomas. SLN biopsy is recommended for patients with intermediate thickness cutaneous melanomas (Breslow thickness, 1 to 4 mm) of any anatomic site. Routine use of SLN biopsy in this population provides accurate staging, with high estimates for proportion successfully mapped (PSM) and acceptable estimates for false-negative rate (FNR), post-test probability negative (PTPN) and predictive value positive (PVP).

Thick Melanomas. Although there are few studies focusing specifically on patients with thick melanomas (T4; Breslow thickness >4 mm), use of SLN biopsy in this population may be recommended for staging purposes and to facilitate regional disease control.

Thin Melanomas. There is insufficient evidence to support routine SLN biopsy for patients with thin melanomas (T1; Breslow thickness <1 mm), although it may be considered in selected patients with high-risk features when the benefits of pathologic staging may outweigh the potential risks of the procedure. Such risk factors may include ulceration or mitotic rate $\geq 1/\text{mm}^2$, especially in the subgroup of patients with melanomas 0.75 to 0.99 mm in Breslow thickness.

Clinical Question 2

What Is the Role of Completion Lymph Node Dissection (CLND)?

CLND is recommended for all patients with a positive SLN biopsy. CLND achieves regional disease control, although whether CLND after a positive SLN biopsy improves survival is the subject of the ongoing Multicenter Selective Lymphadenectomy Trial II (MSLT II).

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Newly diagnosed melanoma

Guideline Category

Assessment of Therapeutic Effectiveness

Evaluation

Management

Treatment

Clinical Specialty

Dermatology

Family Practice

Internal Medicine

Nuclear Medicine

Oncology

Pathology

Surgery

Intended Users

Physicians

Guideline Objective(s)

To provide an evidence-based guideline on the use of lymphatic mapping and sentinel lymph node (SLN) biopsy in staging patients with newly diagnosed melanoma

Target Population

Patients diagnosed with newly diagnosed melanoma

Interventions and Practices Considered

1. Sentinel lymph node biopsy (SNL)
2. Completion lymph node dissection (CLND)

Major Outcomes Considered

- Staging accuracy as measured by proportion successfully mapped (PSM), false-negative rate (FNR), post-test probability negative (PTPN), and predictive value positive (PVP)
- Same nodal basin, regional, or distant recurrence
- Regional disease control
- Risks of the procedure/surgical morbidity

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Strategy

A comprehensive systematic review of the literature was completed, and a detailed description of the systematic review methodology, including the quality appraisal of the evidence and quality control measures, has been published elsewhere. In summary, the initial systematic review included literature published from January 1990 through December 2009. MEDLINE and EMBASE were searched using the search terms "melanoma" and "sentinel lymph node." An updated literature search was conducted to review articles published since the initial search to ensure that none of the guideline recommendations would need to be changed after consideration of any new evidence. This second updated review included a search for publications from December 2009 through August 2011. The searches were supplemented with the references of the selected articles, abstracts presented at American Society of Clinical Oncology (ASCO) and Society of Surgical Oncology (SSO) annual meetings in the last 5 years, and references provided by guideline Panel members.

Inclusion and Exclusion Criteria

Studies were required to report the number of patients in whom sentinel lymph node (SLN) biopsy was attempted, the number who had successful identification and removal of an SLN, and continuous follow-up for the group of patients who had a negative SLN biopsy. No exclusion was made based on Breslow thickness, type of study, or whether the study was retrospective or prospective in nature. However, the population reported had to be original. When a single institution had multiple reports on its populations, the report that had the largest population, longest follow-up, and/or more appropriate outcomes was selected. Studies were excluded if they reported only patients with tumor-positive SLN biopsy, referred only to a highly specific population or location, and/or involved ≤ 50 patients.

Number of Source Documents

73 studies met full eligibility criteria

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Meta-Analysis

Systematic Review

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Two reviewers independently assessed the quality of the selected studies using the criteria from the Methodological Index for Non-Randomized Studies. No article was excluded based on the quality assessment, but a sensitivity analysis was performed to estimate the effects of quality on the estimates.

Meta-Analysis

A meta-analysis (see the "Availability of Companion Documents") was conducted based on the results of the initial systematic review of the literature (i.e., including literature published from January 1990 through December 2009). Primary outcomes consisted of measures of test performance, including: the proportion successfully mapped (PSM), false-negative rate (FNR), post-test probability negative (PTPN), and predictive value positive (PVP) using same nodal basin recurrence as the outcome of interest. The PSM was defined as the ratio between the number of patients who had at least one sentinel lymph node (SLN) excised and the total number of patients included in the study. Specifically, for the calculation of the FNR, the following formula was used: $FN/(TP + FN)$, where $FNR = \text{patients with regional recurrence after negative SLN biopsy} / (\text{patients with positive SLN biopsy regardless of recurrence} + \text{patients with regional recurrence after negative SLN biopsy})$. PTPN was calculated as the ratio of patients with negative SLN biopsy who experienced recurrence to all patients with negative SLN biopsy. This is equivalent to 1-predictive value negative of the test. PVP was calculated as the ratio of patients with positive SLN biopsy with recurrence, divided by all patients with positive SLN biopsy. Secondary outcomes included the results of completion lymph node dissection (CLND) and the same measurements of test performance as for primary outcomes, focusing on regional recurrences with or without distant metastases.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The American Society of Clinical Oncology (ASCO) and Society of Surgical Oncology (SSO) convened a Panel consisting of expert surgeons and medical oncologists from both societies. The Panel also included experts in nuclear medicine, pathology, and patient advocacy.

The entire Panel met in February 2010 to review the evidence and draft the guideline recommendations. Additional work on the guideline was completed through a steering group and by email. All members of the Panel participated in the preparation of the draft guideline document.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Feedback from external reviewers was solicited, and the guideline was submitted to Journal of Clinical Oncology (JCO) and Annals of Surgical Oncology (ASO) for peer review. Before publication, the guideline was reviewed and approved by the American Society of Clinical Oncology (ASCO) Clinical Practice Guidelines Committee and Society of Surgical Oncology (SSO) Executive Council and reviewed by the SSO Melanoma Disease Site Work Group.

American Society of Clinical Oncology Clinical Practice Guidelines Committee and Society of Surgical Oncology Executive Council approval: March 21, 2012.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting each recommendation is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Improved identification of patients for whom the expected benefits of sentinel lymph node (SNL) biopsy and completion lymph node dissection (CLND) outweigh the risks of surgical morbidity
- Improved staging accuracy
- Regional disease control
- Improved survival

Potential Harms

- Clinical judgment must be used when considering sentinel lymph node (SLN) biopsy in patients with comorbid medical conditions. The individual risks and benefits of the procedure should be weighed against the operative and anesthetic risks as well as potential competing causes of mortality.
- Complications after SLN biopsy are uncommon. The overall complication rate reported in Multicenter Selective Lymphadenectomy Trial (MSLT) I was 10.1% after SLN biopsy (n= 937) compared with 32.7% after completion lymph node dissection (CLND) (n=234). The most common complications after SLN removal documented in MSLT I included seroma (5.5%), infection (4.6%), and wound separation (1.2%). The Sunbelt Melanoma Trial (also a prospective randomized trial) similarly showed a low overall rate of complications from SLN biopsy (4.6%) compared with CLND (23.2%). Most complications were noted to be short-term issues that resolved over time with wound care and selective use of antibiotics.
- CLND is associated with risks of long-term morbidity, especially lymphedema. However, morbidity with CLND may be considerably worse when it is delayed until there is clinically evident disease. In a study comparing patients who underwent inguinal lymph node dissection for tumor-positive SLNs compared with palpable nodal metastases, wound complications (28% v 14%; P = .02) and lymphedema (41% v 24%; P = .025) were significantly greater after CLND among patients with palpable nodal disease compared with those with a positive SLN. The observed increases in morbidity for patients who have undergone therapeutic lymphadenectomy for palpable disease and the increased morbidity associated with radiation therapy support the continued use of CLND for patients with a positive SLN biopsy rather than delayed CLND for palpable disease. Analysis of MSLTI also found that the number of positive nodes and lymphedema risk were greater for patients who underwent lymphadenectomy for clinically evident nodal disease compared with those who underwent CLND for positive SLNs.
- In pregnant women, if sentinel lymph node (SLN) biopsy is performed, use of radioactive tracer for lymphoscintigraphy seems safe, although attendant risks of exposure to a low amount of radioactivity should be discussed. Risks from blue dye injection are unknown, so it is not recommended for SLN biopsy in patients who are pregnant because of the possibility of anaphylactic shock.

Qualifying Statements

Qualifying Statements

This practice guideline is not intended to substitute for the independent professional judgment of the treating physician. Practice guidelines do not account for individual variation among patients and may not reflect the most recent evidence. This guideline does not recommend any particular product or course of medical treatment. Use of the practice guideline is voluntary. Additional information is available at the [American Society of Clinical Oncology website](#) .

Limitations of the Literature

There is currently only one randomized controlled trial (MSLT I) that addresses whether patients with melanoma managed using sentinel lymph node (SLN) biopsy have better clinical outcomes than those whose disease is managed with nodal observation. Hence, observational studies were included in the systematic review of the literature. Because there was significant variability and complexity across the many uncontrolled clinical trials, the systematic review included cohort studies of patients with melanoma who underwent SLN biopsy with or without completion lymph node dissection (CLND) and who were observed for evidence of same nodal basin, regional, or distant recurrence. Readers should be cautious when considering aggregate data, because there was significant variability across the studies identified in the systematic review, including surgical, pathologic, and nuclear medicine techniques, which have evolved substantially over time.

Implementation of the Guideline

Description of Implementation Strategy

For information on the American Society for Clinical Oncology (ASCO) implementation strategy, please see the [ASCO Web site](#) .

Implementation Tools

Patient Resources

Resources

Slide Presentation

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 Jul 9

Guideline Developer(s)

American Society of Clinical Oncology - Medical Specialty Society

Society of Surgical Oncology - Medical Specialty Society

Source(s) of Funding

American Society of Clinical Oncology

Guideline Committee

Joint Expert Panel from the American Society of Clinical Oncology and Society of Surgical Oncology

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Guideline and Conflicts of Interest

The Expert Panel was assembled in accordance with the American Society of Clinical Oncology (ASCO) Conflict of Interest Management Procedures for Clinical Practice Guidelines (summarized at <http://www.asco.org/guidelinescoi>). Members of the Panel completed a disclosure form, which requires disclosure of financial and other interests that are relevant to the subject matter of the guideline, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as the result of promulgation of the guideline. Categories for disclosure include employment relationships, consulting arrangements, stock ownership, honoraria, research funding, and expert testimony. In accordance with the Procedures, the majority of the members of the Panel did not disclose any such relationships.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the [American Society of Clinical Oncology \(ASCO\) Web site](#) .

Print copies: Available from American Society of Clinical Oncology, Cancer Policy and Clinical Affairs, 2318 Mill Rd, Suite 800, Alexandria, VA 22314; E-mail: guidelines@asco.org

Availability of Companion Documents

The following are available:

- Sentinel lymph node biopsy for melanoma: American Society of Clinical Oncology and Society of Surgical Oncology joint clinical practice guideline. Data supplements. 2012. 10 p. Electronic copies: Available in Portable Document Format (PDF) from the [American Society of Clinical Oncology \(ASCO\) Web site](#) .
- Sentinel lymph node biopsy for melanoma: American Society of Clinical Oncology and Society of Surgical Oncology joint clinical practice guideline. Appendix. 2012. 12 p. Electronic copies: Available in Portable Document Format (PDF) from the [ASCO Web site](#) .
- Sentinel lymph node biopsy for melanoma: American Society of Clinical Oncology and Society of Surgical Oncology joint clinical practice guideline. Slide set. 2012. 12 p. Electronic copies: Available in [Portable Document Format \(PDF\)](#) and

[PowerPoint](#) from the ASCO Web site.

- Lymphatic mapping and sentinel lymph node biopsy in patients with melanoma: A meta-analysis. American Society of Clinical Oncology; 2011. 9 p. Electronic copies: Available in Portable Document Format (PDF) from the [ASCO Web site](#) .

Patient Resources

The following is available:

- What to know: the ASCO and SSO guideline on sentinel lymph node biopsy for melanoma. Alexandria (VA): American Society of Clinical Oncology; 2012 Jul. Electronic copies: Available from the [American Society of Clinical Oncology Web site](#) .

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NGC Status

This NGC summary was completed by ECRI Institute on August 1, 2012. This summary was updated by ECRI Institute on February 15, 2017 following the U.S. Food and Drug Administration advisory on general anesthetic and sedation drugs.

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